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An Appreciation of Free Radicals

I – Introduction

An Ocean of Free Radicals

Free radicals are chemical entities that are perhaps the most misunderstood by our undergraduate students and teachers. (This statement stems from my experience of lecturing to undergraduate teachers participating in the UGC Refresher courses in several universities). The purpose of this article is to dispel the misconceptions, and to bring to the attention of the *Resonance* readers the great significance of free radicals in diseases and health, environmental quality, and such other vital aspects that touch us in every way, in addition to their important role in chemical industry and synthetic chemistry. Many may be surprised to know that we are actually living in an ocean of free radicals, because, not only is atmospheric oxygen a free radical that contains two unpaired electrons, but a great number of radicals are generated and destroyed continuously in the environment by natural processes and human activities. The involvement of free radical processes in cancer, heart diseases, ageing, Alzheimer's and Parkinson's diseases, inflammations, etc., is considered very likely as shown by numerous research findings. The formation of the hole in the ozone layer is directly related to the chemistry of atmospheric free radicals. A large number of chemical industries also depend on free radical reactions. (Radical polymerisation reactions are employed in the manufacture of three quarters of all polymers produced!) It is therefore needless to emphasise that a tremendous effort is expended in the area of free radical research in medicine, chemistry and environment.

What is a Free Radical?

A free radical can be defined as any chemical entity, i.e., an atom or a compound that has one or more unpaired electrons. This means that a wide range of chemical species, from such simple ones as hydrogen, halogens, to simple molecular species like

Keywords

Free radicals, chain reactions, reactive intermediates, radicals in environment.



$\cdot\text{CH}_3$, $\cdot\text{CH}_2\text{-CH}_3$, O_2 , NO , to very complex species can exist as free radicals.

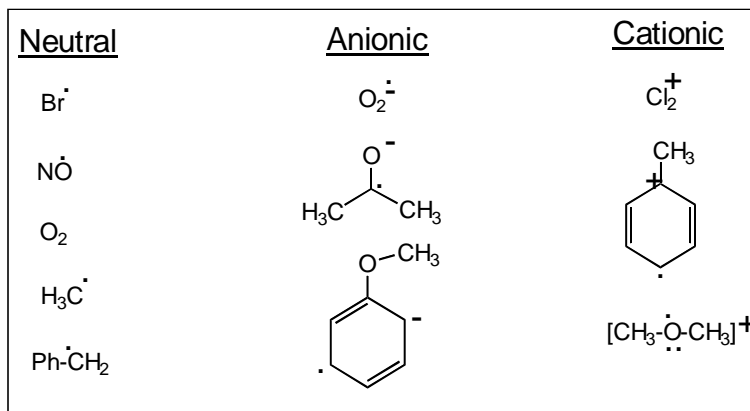
A free radical can be a neutral, negatively charged (radical anion) or positively charged (radical cation) species (*Structure 1*).

Contrary to common belief among undergraduate teachers and students, not all free radicals are very reactive. In fact,

the reactivity varies so widely that while some free radicals react instantaneously, some others may remain unreacted for years. In this sense, organic free radicals are quite different from carbanions and carbocations, in that they are not necessarily always reactive intermediates, but may exist as stable products in their own right. Both steric effects and electronic effects contribute to the stability of free radicals.

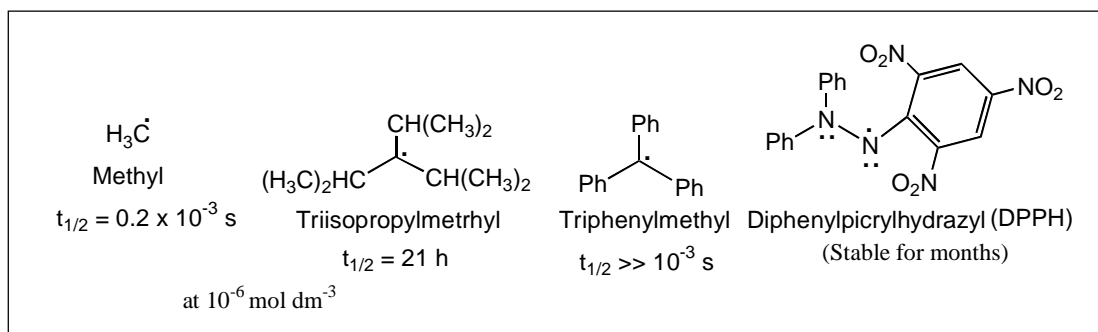
Why are they called Free Radicals?

A radical, in general terms, is a root or base or source of a structure or quantity (as in botany and mathematics). In the mid-nineteenth century, when structural chemistry was still largely unknown, inorganic salts such as sodium chloride, potassium sulphate, silver nitrate, etc., were analysed for sodium and chloride radicals, potassium and sulphate radicals, or silver



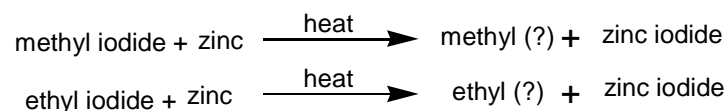
Structure 1.

Structure 2.

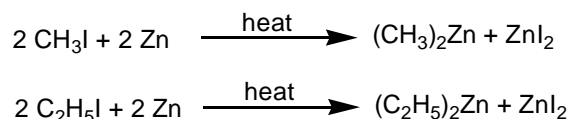


Frankland serendipitously initiated a whole new area of chemistry called 'Organometallic Chemistry'.

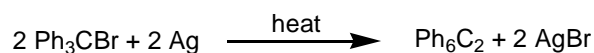
and nitrate radicals, as we do even today. This idea seems to have been extended to organic compounds also, in the absence of a good structural theory at the time. Therefore, ethyl bromide would consist of an ethyl radical and a bromide (bromine) radical, and iodobenzene would contain a phenyl radical and an iodide (iodine) radical. It was then conceivable to chemically separate or free the ethyl radical (or any other radical like methyl, propyl, etc.) from the other radical (bromide, iodide, etc.). This was indeed attempted for the first time by Frankland in 1848 by heating methyl iodide and ethyl iodide with zinc, assuming that zinc would remove iodine and free the methyl and ethyl radicals.



However, Frankland failed to get the methyl or ethyl free radical, but he serendipitously initiated a whole new area of chemistry called 'Organometallic Chemistry' by preparing dimethyl zinc and diethyl zinc in his experiments. We now represent the above reactions in the form of the following equations.



Ultimately, it was in 1900 that Gomberg demonstrated the existence of free radicals while studying the following reaction.



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In this reaction, an initially formed yellow coloured intermediate, proposed as triphenylmethyl radical (Ph_3C) by Gomberg, gave the product Ph_6C_2 , which he wrongly thought as hexaphenyl-ethane. (Note that the electron had been discovered just three years before and its role in chemical bonding was still not known. The correct structure of Ph_6C_2 was established a few decades later).

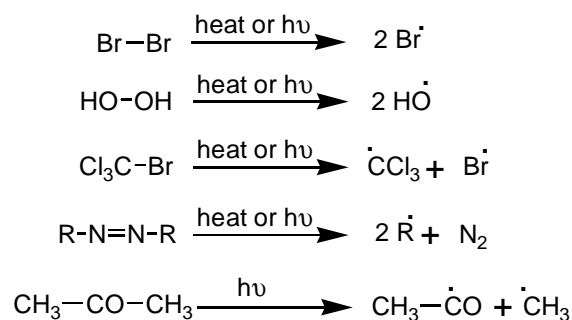


How do we get Free Radicals?

Since the presence of an odd electron in an atom or molecule confers it the free radical status, this can be achieved in many ways.

1. Homolysis of a Covalent Bond

A covalent bond can be homolytically cleaved by supplying appropriate energy (bond dissociation energy) in the form of heat or light. Weaker bonds are broken more easily, and this is the most common method of generating free radicals either by heat or light including solar radiation.



Since any activity that results in homolysis of a covalent bond is a source of free radicals, both natural phenomena and human activities can produce huge quantities of free radicals. Some of these are listed here.

- Burning of organic matter, as in the case of
 - (a) Forest fires
 - (b) Automobile, aviation, boiler fuels
 - (c) Wood, gas, kerosene, etc., during cooking
 - (d) Smoking (A single puff of cigarette smoke is known to contain 10^{14} free radicals.)

One can only imagine the number of free radicals collectively produced by all these processes.

- Chemical decomposition by solar UV radiation. This is

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Bond	Energy (kJ mol ⁻¹)
C-H in hydrocarbons	360 - 520
C-C in hydrocarbons	300 - 450
O-O in peroxides	150 - 210
O-NO in nitrites	170 - 180
C-Cl	320 - 350
C-Br	260 - 280
Cl-Cl	242
Br-Br	193
C-NO	167 - 175
H-OH	498
CO-Cl	230 - 250

Table 1.

responsible for most of the free radical reactions taking place in the biosphere and atmosphere including the preservation of ozone balance.

- Radioactivity produces high-energy particles and high-energy radiation, both of which can decompose chemicals and generate free radicals.
- Volcanic activities throw up huge quantities of free radicals.
- Lightning is another important natural phenomenon that produces enormous

quantities of free radicals, particularly the oxides of nitrogen.

- In living organisms, metabolic activities generate free radicals. Illness causes the body to produce harmful radicals.

Homolytic cleavage is the main source of free radicals. Hence a good knowledge of the bond dissociation energies of various covalent bonds and the factors influencing the stability of the radicals formed is essential for understanding the free radical reactions. Some bond dissociation energies useful in this context are listed in Table 1.

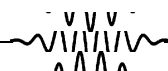
2. Using one Radical to Generate Another

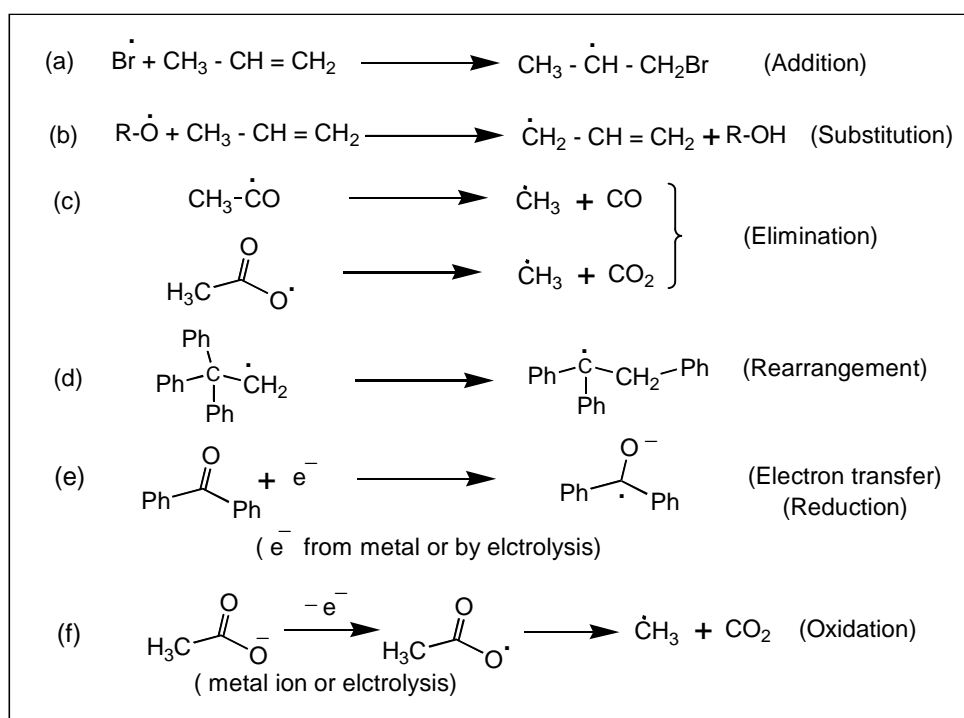
Free radicals, including oxygen, can react in many ways, either intermolecularly or intramolecularly, to produce other free radicals. This is an integral part of a radical chain process. Some examples are given in Scheme 1.

Reactivity of Free Radicals

The first half of the twentieth century witnessed a rather slow development of free radical chemistry. This was because, unlike ionic reactions, most free radical reactions yielded complex mixtures of products, which were difficult to analyse and interpret on the one hand, and were not practical for preparative purposes

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on the other. The free radicals involved in these reactions were not only very reactive, but very little was understood about their behaviour; the reactions were virtually allowed to take their own course. The situation has changed vastly, so much so that free radicals have been tamed to take a desired reaction course.

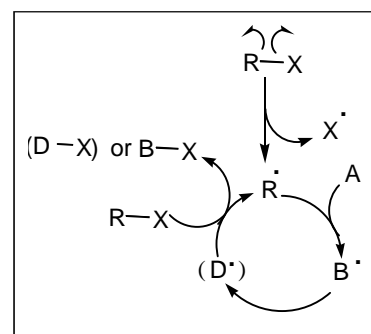
Scheme 1.

General Features of a Free Radical Reaction

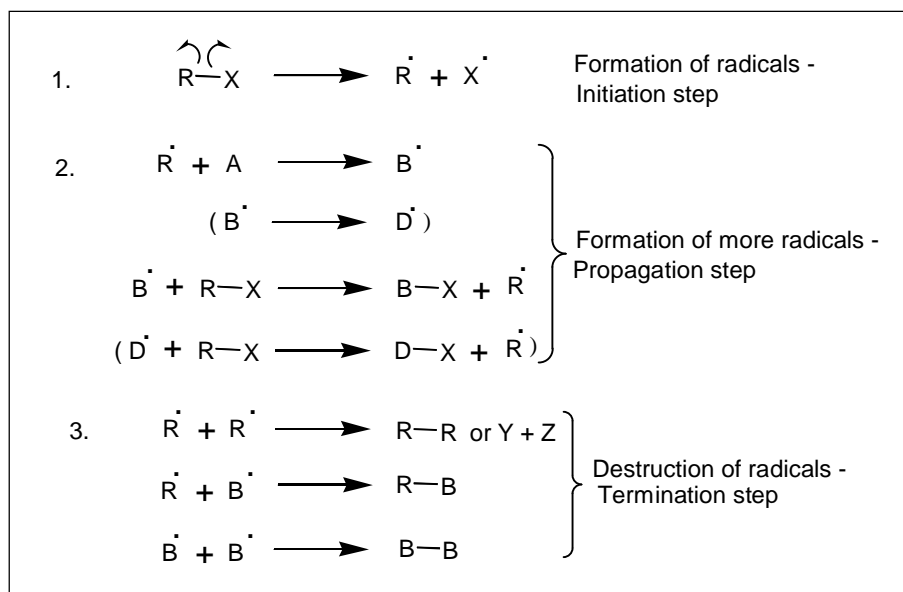
In any case, free radical reactions take three distinct, identifiable steps (Scheme 2).

The second step, the propagation, is the heart of a free radical reaction. A good understanding and control of this step will deliver the desired results. In this step, the required free radical $\text{R}\cdot$ is regenerated repeatedly, which would take the reaction to completion, if there were no intervention of the third (termination) step. Because of this repetitive nature of the reaction, it is called 'Chain Reaction' and is often represented as a cyclic process, Figure 1.

Figure 1.



From humble beginnings at the dawn of the twentieth century,

**Scheme 2.**

free radical chemistry has spread its influence over a wide range of research areas that impinge on our progress and well being. Apart from polymer chemistry, synthetic organic chemistry and environmental chemistry, much effort in recent times is expended on research in health and nutrition. The importance of the latter can be gauged by the fact that there is a 'Society of Free Radical Research of India' formed by the medical fraternity devoted exclusively to research in this area.

In subsequent parts, industrial applications of free radical chemistry, organic synthesis using free radicals, free radicals in human health, environmental aspects including the chemistry behind the ozone hole will be considered. A few simple experiments involving free radical reactions will also be given.

